

REMARKS

Entry of the foregoing, reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

I. Claim Amendments

By the foregoing amendments to the claims, claim 1 has been amended and claim 2 been cancelled.

In particular, claim 1 has been amended to recite the subject matter of claim 2 (*i.e.* that the pentose is a pentose in (3S, 4R) or (3R, 4S), and that the pentose-5-phosphate ester is a pentose-5-phosphate ester in (3S, 4R) or (3R, 4S)).

The amendments to the claims, including cancellation of claims, have been made without prejudice or disclaimer to any subject matter recited or canceled herein. Applicants reserve the right to file one or more continuation and/or divisional applications directed to any canceled subject matter. No new matter has been added, and entry of the foregoing amendments to the above-identified application are respectfully requested.

II. Response to Claim Rejections Under 35 U.S.C. § 103

Claims 1-8 have been rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over Tanaka et al. (Org. Biomol. Chem. 1:2833-2839 (July 9, 2003)) in view of Gross et al. (J. Am. Chem. Soc. 105:7428-7435 (1983)). This rejection is respectfully traversed.

To expedite prosecution in the present application, and not to acquiesce to the Examiner's rejection, the claims have been amended as described above. Applicants submit that the cited references, taken alone or together, do not teach or suggest the subject matter of the present claims, for at least the following reasons.

The present inventors have unexpectedly discovered a process comprising phosphorylation of a free pentose with the use of an acid phosphatase. In the present application, the inventors studied the substrate specificity of acid phosphatase for various pentoses, and surprisingly discovered that pentoses capable of serving as substrates for acid phosphatase have a particular steric structure on the 5-OH of the reacting site and comprise 4- and 3- OH. As recited in the claims, the present inventors found that suitable pentoses are

classified in (3S, 4R) or (3R, 4S).

In contrast to the present application, Tanaka et al. describe selective phosphorylation of glucose and do not teach or suggest phosphorylation of a free pentose. In this regard, Applicants note that whether a compound is suitable as an enzyme substrate depends on the substrate specificity of the enzyme, which is highly unpredictable. Even where two compounds may have some apparent structural similarity, those two compounds are not necessarily effective substrates for a common enzyme. Thus, even if glucose was known as a substrate for an acid phosphatase, the reactivity of pentose could not be predicted, because the substrate specificity of the acid phosphatase had not been tested and was not known in the art. In particular, the specificity of pentose phosphate for pentose in (3S, 4R) or (3R, 4S) was not known in the art prior to the present invention.

The art at the time of filing supports the position that it is difficult to predict whether or not a particular sugar will be a substrate of a particular enzyme. For example, Xu et al., *Biochem.* 34:6083-6092 (1995) (a copy of which has been submitted herewith) show that although glucose (carbon number: 6) is a suitable substrate for glucokinase, mannoheptulose (carbon number: 7) is not, even though mannoheptulose also has high polarity and might therefore have been expected to have an enzyme reactivity similar to that of glucose. In addition, Hansen et al., *J. Bacteriol.* 184:5955-5965 (2002) (also submitted herewith), studied the effectiveness of various hexoses as substrates for glucokinase and hexokinase, and found that the reactivity of the hexoses with the enzymes varied significantly depending on the particular combination of sugar and enzyme.

As noted above, the present inventors found that suitable pentoses are classified in (3S, 4R) or (3R, 4S). On the other hand, pentoses not suitable as substrates for acid phosphatase are classified in (3R, 4R). In contrast, hexoses did not follow this pattern. Further, as shown in Example 2 (FIG. 1) of the present application, deoxyribose is poorly phosphorylated under conditions similar to the glucose phosphorylation conditions of Tanaka et al. (i.e. 100mM glucose, 100 mM sodium pyrophosphate), demonstrating that a one-carbon difference in carbon number can drastically change the reactive yield (glucose: not less than 30%, deoxyribose: 1%). Thus, although hexose and pentose both have hydroxyl groups and high polarity, a person of ordinary skill in the art would not have reasonably predicted that pentose would be an effective substrate for acid phosphatase.

Tanaka et al. also describes selective phosphorylation of inosine. However, as shown

in Ishikawa et al., Protein Eng. 15:539-543 (2002) (submitted herewith), the presence of hypoxanthine coordinated first place of inosine is important for the recognition of inosine as a substrate, for orientation control and for the reaction of inosine with acid phosphatase (see FIG.1, 2nd paragraph of page 541, 2nd paragraph of page 542, and Table 2 of Ishikawa et al.). Accordingly, a person of ordinary skill in the art would not have expected free pentose to be useful as an acid phosphatase substrate, because free pentose is not modified by hypoxanthine.

Finally, Gross et al. does not teach or suggest preparing a pentose-5-phosphate ester. The process described in Gross et al. and cited by the Examiner (right column of page 7429, the second line from the bottom) is a process for producing ribose-5-phosphate ester by using ATP as phosphate donor and ribokinase as enzyme. Thus, the process disclosed in Gross et al. is completely unrelated to the present invention, and Gross et al. does not remedy the serious deficiencies of Tanaka et al.

For at least these reasons, the present process would not have been obvious to a person of ordinary skill in the art, and Applicants thus respectfully request reconsideration and withdrawal of the 35 U.S.C. § 103(a) rejection.

CONCLUSION

From the foregoing, favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions related to this response, or the application in general, it would be appreciated if the Examiner would telephone the undersigned attorney at the below-listed telephone number concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

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